



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

## NOTICE OF ALLOWANCE AND FEE(S) DUE

959 7590 09/30/2011  
NELSON MULLINS RILEY & SCARBOROUGH LLP  
FLOOR 30, SUITE 3000  
ONE POST OFFICE SQUARE  
BOSTON, MA 02109

EXAMINER

KAM, CHIHMIN

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 09/30/2011

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,536	06/16/2006	Christian Widmann	KZY-004US	8023

TITLE OF INVENTION: RASGAP DERIVED PEPTIDE FOR SELECTIVELY KILLING CANCER CELLS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$870	\$300	\$0	\$1170	12/30/2011

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE** OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

## HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to: Mail**

**Mail Stop ISSUE FEE  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
or Fax (571)-273-2885**

**INSTRUCTIONS:** This form should be used for transmitting the **ISSUE FEE** and **PUBLICATION FEE** (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

959 7590 09/30/2011  
**NELSON MULLINS RILEY & SCARBOROUGH LLP**  
FLOOR 30, SUITE 3000  
ONE POST OFFICE SQUARE  
BOSTON, MA 02109

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,536	06/16/2006	Christian Widmann	KZY-004US	8023

TITLE OF INVENTION: RASGAP DERIVED PEPTIDE FOR SELECTIVELY KILLING CANCER CELLS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$870	\$300	\$0	\$1170	12/30/2011

EXAMINER	ART UNIT	CLASS-SUBCLASS
KAM, CHH MIN	1656	514-002000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB-112) attached;  
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB-112, Rev. 03-02 or more recent) attached. Use of a **Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, \_\_\_\_\_  
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. \_\_\_\_\_  
\_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.111. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee  
☐ Publication Fee (No small entity discount permitted)  
☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s): (Please first reuply any previously paid issue fee shown above)

- ☐ A check is enclosed.  
☐ Payment by credit card. Form PTO-2038 is attached.  
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

- ☐ a. Applicant claims **SMALL ENTITY** status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming **SMALL ENTITY** status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_ Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_ Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.**

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,536	06/16/2006	Christian Widmann	KZY-004US	8023

959 7590 09/30/2011  
NELSON MULLINS RILEY & SCARBOROUGH LLP  
FLOOR 30, SUITE 3000  
ONE POST OFFICE SQUARE  
BOSTON, MA 02109

EXAMINER

KAM, CHIH MIN

ART UNIT	PAPER NUMBER
----------	--------------

1656

DATE MAILED: 09/30/2011

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 287 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 287 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

## Privacy Act Statement

**The Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

**Notice of Allowability****Application No.**

10/563,536

**Applicant(s)**

WIDMANN ET AL.

**Examiner**

CHIH-MIN KAM

**Art Unit**

1656

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 3/7/2011.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_\_; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are 1-9, 11, 12, 14, 15, 17-19, 23, 27-31 and 33-65.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some\* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 3/7/2011
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date \_\_\_\_\_.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_.

/Chih-Min Kam/  
Primary Examiner, Art Unit 1656

### **DETAILED ACTION**

1. The Request for Continued Examination (RCE) filed on March 7, 2011 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

#### ***Status of the Claims***

2. Claims 1-9, 11, 12, 14, 15, 17-19, 23 and 27-65 are pending.

Applicants' amendment filed March 7, 2011 is acknowledged. Applicants' response has been fully considered. Claims 1, 29, 31, 33, 37, 40 and 48-52 have been amended. Therefore, claims 1-9, 11, 12, 14, 15, 17-19, 23 and 27-65 are examined.

#### ***Examiner's Amendment***

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Debra J. Milasincic on September 26, 2011.

#### **Examiner's Amendment to the Claims:**

Cancel claim 32.

Claims 1, 29, 31, 33, 37, 40 and 48-52 have been amended as follows:

1. (Currently amended) A pharmaceutical composition comprising
  - i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and
  - ii) a genotoxin,

wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells.

29. (Currently Amended) A kit for treating cancer in a subject comprising a pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin,

wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells, and instructions for use.

31. (Currently amended) A kit for treating cancer in a subject comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein X represents an amino acid; or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin,

wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells, and instructions for use of said at least one peptide fragment or the retro-inverso form thereof and the genotoxin.

33. (Currently Amended) A method for enhancing apoptosis in a cancer cell, comprising contacting the cancer cell with a therapeutically effective amount of

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin,

wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to selectively kill said cancer cell.

37. (Currently amended) A method for enhancing the sensitivity of a cancer cell to a genotoxin comprising contacting the cancer cell with a genotoxin and a therapeutically effective amount of at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, thereby enhancing the sensitivity of a cancer cell to the genotoxin.

40. (Currently Amended) A method of treating cancer in a subject comprising administering to said subject a therapeutically effective amount of

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin,

wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells, such that said cancer is treated.

48. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin, wherein said genotoxin is a DNA cutter,

and wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells.

49. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at

Art Unit: 1656

least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin, wherein said genotoxin is a topoisomerase poison,

and wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells.

50. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin, wherein said genotoxin is a DNA binder,

and wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells.

51. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin, wherein said genotoxin is a spindle poison,

and wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells.

52. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO: 14), wherein said at

least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide fragment, and

ii) a genotoxin, wherein said genotoxin is an antimetabolite,

and wherein said at least one peptide fragment or the retro-inverso form thereof enhances the ability of said genotoxin to kill selectively cancer cells.

**The following is an Examiner's Statement of Reasons for Allowance:** The following references are the closest art to the claimed invention. Yang *et al.* (Mol. And Cell. Biology 21, 5346-5358 (2001)) teach characterization of RasGAP and its N-fragment (residues 1-455), where N-fragment contain N1 fragment (residues 1-157) and N2 fragment (residues 158-455), the N2 fragment contains 2 SH2 and one SH3 domain (Fig.1; page 5348, right column), and SH3 contains WXWVTXXRTX or instant SEQ ID NO:8 (WMWVTNLRTD). Yang *et al.* also teach N1 and N2 fragments of RasGAP sensitizes HeLa cells (a tumor cell) toward DNA induced apoptosis, where HeLa cells were transfected with plasmid encoding HA-GAP caspase cleavage fragments (i.e., N1 and N2 fragments), and the cells were treated in the presence and absence of cisplatin at various concentrations, it was found that the N fragment, N1 and N2 fragments enhances apoptosis of HeLa cells in the presence of cisplatin. Duchesne *et al.* (WO 94/03597 or U.S. Patent 6,180,362) disclose a peptide consisting of the sequence of WMWVTNLRTD (P5; corresponding to instant SEQ ID NO:8), and peptide fragments of N2 sequence of comprising the sequence of WMWVTNLRTD (P6 or P8), which are capable of inhibiting the transformation activity of the Ras protein; an the use of peptides I pharmaceutical compositions for the treatment of cancer. However, either Yang *et al.* or Duchesne *et al.* do not teach that a pharmaceutical composition comprising i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence of WXWVTXXRTX (SEQ ID NO:14), wherein the at least one peptide fragment is less than 90% of the length of the N2 sequence, and wherein X is an amino acid, or a retro-inverso form of the at least one peptide fragment, and ii) a genotoxin, wherein the at least one peptide fragment or the retro-inverso form thereof enhances the ability of the genotoxin to kill selectively cancer cells; and that a kit for treating cancer comprising the pharmaceutical composition. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached at 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Chih-Min Kam/

Primary Examiner, Art Unit 1656

CMK

September 26, 2011